

**STANFORD UNIVERSITY Research Consent Form**

Protocol Director:

*IRB Use Only*

Approval Date: November 6, 2018

Expiration Date:

Protocol Title : **A Phase 1 study of BPM31510 plus vitamin K in subjects with high-grade glioma that has recurred on a bevacizumab-containing regimen**

Are you participating in any other research studies? \_\_\_\_\_ Yes \_\_\_\_\_ No

**PURPOSE OF RESEARCH**

You are invited to voluntarily participate in a research study of BPM31510, an experimental ("investigational") preparation of ubidecarenone (Coenzyme Q10, CoQ10), being conducted by Seema Nagpal, MD at the Stanford Cancer Center. We hope to learn if BPM31510 is safe at several doses, to find the highest dose of BPM31510 that can be given without causing severe side effects and see if high-grade glioma responds to BPM31510. You were selected as a possible participant in this study because you have previously received bevacizumab to treat your high-grade glioma but the cancer progressed.

If you decide to terminate your participation in this study, you should notify [REDACTED], Protocol Director, at [REDACTED].

This research study is looking for up to 10 people with recurrent high-grade glioma to participate in this study. This study is only being conducted at Stanford University.

**VOLUNTARY PARTICIPATION**

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care to which you are entitled.

**DURATION OF STUDY INVOLVEMENT**

You may continue treatment on this study for as long as you are receiving medical benefit and wish to continue. If you stop treatment, we will follow up with you every 3 months. It is expected that this study will be complete in about 2 years.

**PROCEDURES****Screening Visit**

If you choose to participate, the first activity will be screening to see if you are eligible for this study. Screening information may be collected as early as 28 days before the 1<sup>st</sup> dose of BPM31510 (Cycle 1, Day 1), but some tests may need to be repeated within specific amounts of time before Cycle 1, Day 1, as indicated below.

- Medical and cancer history
- Physical examination and vital signs (a check of your height, weight, temperature, blood pressure, breathing rate and heartbeat).

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- Blood samples: about 2 tablespoons (30 mL) of blood will be collected to make sure you do not have an infection, your blood clotting is normal and your bone marrow and organs are working properly.
- If you are a woman who can become pregnant, we will collect a serum pregnancy test. The pregnancy test must be negative within 7 days before the 1<sup>st</sup> dose of BPM31510 (Cycle 1, Day 1).
- Urine sample will be collected to see the health of your body before starting.
- Magnetic Resonance Imaging (MRI) with contrast of your brain within 21 days before Cycle 1, Day 1.
- A positron emission tomography (PET) scan (which will include a non-contrast head CT) will be performed within 14 days before Cycle 1, Day 1. A PET scan is a computerized image that looks at blood flow and the extent and activity of the cancer in your brain. A tourniquet will be applied to your arm or leg to help find a vein, and a small amount of a radioactive tracer called <sup>18</sup>F-FDG (<sup>18</sup>F-fluorodeoxyglucose) will be injected into a vein about 1 hour before the scan. The radiolabel accumulates in areas of the body that are metabolically active, and this accumulation is detected by the scanner. You will be asked to lie on a long narrow bench for up to 45 minutes while the machine performs the scan. You will be asked to not eat or drink anything but water (ie, "fast") for about 4 to 6 hours before the scan. The entire procedure will take about 30 to 60 minutes. You may experience some discomfort or anxiety from being in the confined space. If this bothers you too much, the study team may provide you with a medication to help you stay calm.
- Peripherally inserted central catheter (PICC line) (long, slender, flexible tube that is inserted into your vein in our upper arm) placement for infusing the study drug.

The Study Team will start tracking your medications at the Screening Visit.

**Study Treatment**

This is an open-label, non-randomized, single-arm trial. That means that everyone will get the same treatment on this study, except some patients may receive a higher or lower dose of BPM31510. Dose levels of BPM31510 in this trial include 88 mg/kg, 110 mg/kg, 137 mg/kg and 171 mg/kg. As of June 2018, patients will only be getting 88 mg/kg or 110 mg/kg.

BPM31510 will be given in 28 day cycles. You will receive BPM31510 as a continuous intravenous ("IV") infusion over 72 hours twice a week. BPM31510 will be placed into a reservoir in a pump that you will carry with you as you go about your daily activities, for example, in a shoulder bag. The pump will continuously deliver BPM31510 via the PICC line in your arm. You will need to come into the clinic twice-a-week to get the pump re-filled, and to have medical tests.

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Participants will receive prophylactic Vitamin K for preventive measures once a week (unless there is a contra-indication) to help stabilize the clotting factors in your blood and prevent bleeding events.

**Study Evaluation Procedures**

During the treatment period, you will come into the clinic twice-a-week to get the BPM31510 infusion pump re-filled, and to have medical tests. In Cycle 1 you will have to come for an extra day (Day 7). Generally the visits will be on Tuesdays and Fridays, but may vary. The following tests and procedures will be conducted each cycle unless otherwise specified:

- Physical exam on Day 1
- Vital signs will be taken with each bag change (twice weekly)
- ☐ 2 teaspoons (10ml) of blood will be collected weekly to measure bone marrow and organ function and 1 teaspoon (5 mL) of blood will be collected twice a week for coagulation testing
- Cycle 1 only, you will have timed blood and urine tests for research purposes
  - Day 1 and 4, Blood work up to 4 hours after bag is changed (total 4 tablespoons/60ml) and urine (4 tablespoons/60ml)
  - Day 7, blood when the infusion ends up to 4 hours later (total 3 tablespoons/45 ml) and urine (4 tablespoons/60ml)
  - Day 8, 15, and 22 blood work up to 2 hours after bag change (total 2 tablespoons/30ml)
  - Day 11, 18 and 25 blood work before each bag change (1 tablespoon/15 ml) and urine (4 tablespoons/60ml)
- Electrocardiogram (ECG or EKG) will be performed on Cycle 1 Days 1, 4, and 22 to measure and record the electrical activity of your heart
- ☐ Prophylactic Vitamin K every week, unless contraindicated.
- ☐ Refill BPM31510 pump twice a week
- ☐ Non-contrast head CT on Cycle 1 Day 28
- ☐ MRI will be conducted Day 1 of all odd cycles
- ☐ PET-CT scan at Cycle 3 Day 1

**End-of-Study / Follow-Up Procedures**

About 30 days after you discontinue BPM3150, you will have the following tests or procedures performed.

- Physical examination.
- Vital signs
- ECG.
- About 2 tablespoons (30 mL) of blood will be collected to measure bone marrow, organ and clotting function.
- Urine collection.

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**Study Long-term Follow-Up Procedures**

The study team will contact you by telephone or review your chart about every 3 months

**MRI (Magnetic Resonance Imaging)**

MRI machines use a strong magnet and radiofrequency magnetic fields to make images of the body interior. The scanning procedure is very much like an X-ray or CT scan. You will be asked to lie on a long narrow couch for 30-60 min while the machine gathers data. During this time you will not be exposed to x-rays, but rather a strong magnetic field and radiofrequency magnetic fields, which you will not feel. You will, however, hear repetitive tapping noises that arise from the Magnetic Resonance scanner. We will provide earplugs or headphones that you will be required to wear. The space within the large magnet in which you lie is somewhat confined, although we have taken many steps to relieve the "claustrophobic" feeling.

**Risks:**

Magnetic fields do not cause harmful effects at the levels used in the MRI machine. However, the MR scanner uses a very strong magnet that will attract some metals and affect some electronic devices. If you have a cardiac pacemaker or any other biomedical device in or on your body, it is very important that you tell the operator/investigator immediately. As metallic objects may experience a strong attraction to the magnet, it is also very important that you notify the operator of any metal objects (especially surgical clips), devices, or implants that are in or on your body before entering the magnet room. All such objects must be removed (if possible) before entering the magnet room. In some cases, having those devices means you should not have an MRI scan performed. In addition, watches and credit cards should also be removed as these could be damaged. You will be provided a way to secure these items. If you have any history of head or eye injury involving metal fragments, if you have ever worked in a metal shop, or if you could be pregnant, you should notify the operator/investigator. You should also notify the operator/investigator if you have any tattoos on your body, including eyeliner and other permanent makeup. Tattoos could become warm and irritated during the scan and remain so for several days. If you would prefer not to participate in the MR scan due to the presence of tattoos on your body, please inform a research team member.

There is a possibility that you will experience a localized twitching sensation due to the magnetic field changes during the scan. This is not unexpected and should not be painful. However, you may have the scan stopped at any time if this occurs.

If you have had a previous reaction to Gadolinium-based contrast agents or a history of severe allergies, please notify the operator/investigator. If you have kidney problems, please tell the operator.

It has been observed that deposits of Gadolinium-based contrast agent (GBCA) remain in the brains of some people who undergo four or more contrast enhanced MRI scans, long

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after the last administration. It is not yet known whether these Gadolinium deposits are harmful or can lead to adverse health effects. You should talk to the study doctor if you have any questions about the use of GBCAs with MRIs.

Dizziness or nausea may occur if you move your head rapidly within the magnet.

**IF YOU FEEL DISCOMFORT AT ANY TIME, NOTIFY THE OPERATOR AND YOU CAN DISCONTINUE THE EXAM AT ANY TIME.**

**Women of Childbearing Potential**

If you are a woman who is able to become pregnant, it is expected that you will use an effective method of birth control to prevent exposing a fetus to a potentially dangerous agent with unknown risk. If you are pregnant or currently breast feeding, you may not participate in this study. You understand that if you are pregnant, if you become pregnant, or if you are breast-feeding during this study, you or your child may be exposed to an unknown risk.

To confirm to the extent medically possible that you are not pregnant, you agree to have a pregnancy test done before beginning this research study.

You must agree to avoid sexual intercourse or use a birth control method judged to be effective by the investigator and which will not interfere with the proposed investigation. You must accept the risk that pregnancy could still result despite the responsible use of reliable method of birth control. You agree to notify the investigator as soon as possible of any failure of proper use of your birth control method, or if you become pregnant, either of which may result in your being withdrawn from the study.

If you are a man participating in this study and your partner is able to become pregnant, you and your partner must use adequate contraception while you are participating in the study and for at least 30 days after taking your last dose of study medication. Your doctor will discuss with you what methods of birth control are considered adequate. You should inform your study doctor if your partner becomes pregnant.

**Handling of your Blood and Tissue Samples**

Some of your blood and urine samples will be shipped frozen to the study sponsor and stored outside of Stanford for analysis. These samples will be identified by your initials and unique study number ("study identifier") only, and not your full name. This study identifier will be a series of numbers and/or letters. Any of your samples which are used in research may result in new products, tests or discoveries. In some instances, these may have potential commercial value and may be developed and owned by the Investigators, Stanford University and/or others. However, donors of samples do not retain any property rights to the materials. Therefore, you would not share in any financial benefits from these products, tests or discoveries.

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**Tissue Sampling for Genetic Testing**

As part of the analysis on your samples, the investigators may do genetic testing. Genetic research is research that studies genes, including gene characteristics and gene versions that are transmitted by parents to children. Genetic research may include looking at information, such as personal appearance and biochemistry, gene sequences, genetic landmarks, individual and family medical histories, reactions to medications and responses to treatment. Genetic research raises certain questions about informing you of any results. Possible risks of knowing results include: anxiety; other psychological distress; and the possibility of insurance and job discrimination. A possible risk of not knowing includes being unaware of the need for treatment. These risks can change depending on the results of the research and whether there is a treatment or cure for a particular disease.

Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.

You carry a gene for a disease and might consider informing relatives that they, too, might carry the gene.

**PARTICIPANT RESPONSIBILITIES**

As a participant, your responsibilities include:

- Follow the instructions of the Protocol Director and study staff.
- Keep your study appointments. If it is necessary to miss an appointment, please contact the Protocol Director or research study staff to reschedule as soon as you know you will miss the appointment.
- Tell the Protocol Director or research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Tell the Protocol Director or research staff if you believe you might be pregnant or gotten your partner pregnant.
- Ask questions as you think of them.
- Tell the Protocol Director or research staff if you change your mind about staying in the study.

**WITHDRAWAL FROM THE STUDY**

If you first agree to participate and then you change your mind, you are free to withdraw your consent and discontinue your participation at any time. Your decision will

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not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled.

If you decide to withdraw your consent to participate in this study, you should notify Protocol Director [REDACTED]

If you withdraw after starting treatment with the study drugs, your Study Doctor or the study team will ask you to return for the End of Study Visit and to contact you for the Long Term Follow Up. If you do not want the Study Doctor to check on your health status after withdrawing from the study, you should say so. Any information collected before you withdraw will be kept and used to complete the research.

The Protocol Director may also withdraw you from the study and the study medication may be stopped, without your consent for one or more of the following reasons:

- Failure to follow the instructions of the Protocol Director and study staff.
- The Protocol Director decides that continuing your participation could be harmful to you.
- Pregnancy
- You need treatment not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

**POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES**

There are risks, discomforts, and inconveniences associated with any research study. This section describes the reasonably foreseeable risks; discomforts; and inconveniences that you may experience. These deserve careful thought. You should talk with the Study Doctor if you have any questions.

You must tell the Study Doctor or study team about all side effects that you have. If you experience serious problems, you may be asked to return to the study center for more tests.

**Side Effects (Non-laboratory) Considered at least Possibly-related to BPM31510**

• Tiredness (fatigue) (24%)	• Headache (10%)
• Upset stomach (nausea) (8%)	• Fever (8%)
• Chills (6%)	• Pain, swelling or stiffness in joints (arthritis) (4%)

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**Laboratory Side Effects Considered at least Possibly-related to BPM31510**

Overall data suggests the changes in clotting, with increased risk of bleeding, can be associated with BPM31510 treatment, especially in those at risk for such changes (decreased platelet count, increased INR /PTT).

There have also been elevations in certain liver function tests which may indicate liver damage (AST and Alkaline Phosphatase).

**Serious Side Effects in BPM31510 Studies**

• Increased levels of AST in the blood [a liver function test (LFT) indicating liver injury]	• Decreased levels of albumin in the blood (hypoalbuminemia, an LFT indicating liver injury)
• Increased levels of bilirubin (an LFT indicating liver injury)	• Decreasing clotting ability (APTT prolonged and/or INR increased)
• Decreased levels of red blood cells (anemia)	• Elevated levels of calcium in the blood (hypercalcemia)
• Blood in the urine (hematuria)	• Pain, chest
• Pain, back	• Pain, abdominal
• Infection (tumor site)	• Infection, skin
• Infection, lung (pneumonia)	• Excess fluid around the lungs (pleural effusion)
• Decreased blood pressure (hypotension)	

Changes in clotting, with increased risk of bleeding have been seen with BPM31510 treatment. Patients with central nervous system tumors may have an increased risk of tumor bleeding with BPM31510 which could lead to life threatening or fatal brain hemorrhage.

In addition, there are other risks and possible discomforts you might experience from the study procedures. The following discusses procedure risks related only to the research, and does not include risks of procedures that should be discussed as part of your regular medical care.

- **Allergic reactions:** All drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life-threatening. You should get medical help and contact the Study Doctors right away if you think you have any of the following symptoms of a serious allergic reaction: trouble breathing, or swelling of the face, mouth, lips, gums, tongue or neck. Other allergic reactions may include rash, hives, or blisters.

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- **Vitamin K injections:** Temporary “flushing sensations” and “peculiar” sensations of taste have been observed, as well as rare instances of low blood pressure, rapid and weak pulse, profuse sweating, brief hypotension, shortness of breath, and cyanosis (blue skin). Pain, swelling, and tenderness at the injection site may occur. Infrequently— usually after repeated injection—red, hardened, itchy plaques have occurred. There is the possibility of allergic sensitivity which may be severe. There have been deaths associated with injections in the vein or muscle. For this study, it will be injected subcutaneously (under the skin)
- **Blood draws:** A blood draw may cause fainting; inflammation of the vein; stinging, discomfort, or pain; bruising; discomfort; redness; burning; or bleeding at the site where the needle is placed to draw the blood. There is a slight chance of infection. You may feel dizzy or you may faint. If you feel faint, you should immediately lie down to avoid falling.
- **ECG:** Risks from an ECG can include skin irritation and/or a rash from the gel, or from wearing or removing the patches.
- **PICC line:** The following are some of the complications that can be associated with PICC lines:
  - Air Embolism: Air bubbles may enter the blood vessel during insertion of a PICC. This may produce symptoms such as decreased blood pressure; lightheadedness; confusion; increased heart rate; anxiety; chest pain; or shortness of breath.
  - Infection: It is possible for an infection to develop either inside the vessel or surrounding the insertion site where the catheter enters the vein. The symptoms include fever; chills; rapid heart rate; fatigue; muscle aches; weakness; decreased blood pressure; redness, swelling or drainage at site; or elevated white blood cell count.
  - Phlebitis: This is inflammation of the vein where the catheter is inserted. The symptoms include redness; pain at access site; streak formation; swollen vein; or yellow drainage.
  - Catheter Malposition: Malposition can occur during PICC insertion or later due to changes in pressure inside the chest or from catheter position movement. After the insertion of catheter, the position of its tip is confirmed with an x-ray. Confirmation of proper tip placement is required before using the device as a poorly placed catheter can cause serious complications. Securing the PICC catheter is also important to help prevent the catheter from coming out of the vein or movement. Sutures should not be used to secure the catheter to the site as these can lead to complications such as infection at the site or catheter-related bloodstream infections.
  - Thrombus Formation: Any catheter placed in the vascular system increases the risk of clot formation, either in the vessel or in the catheter.
  - Difficult Removal: There may be resistance when removing the catheter and this may occur at any time during the process.

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- Nerve Injury or Irritation: During insertion of the catheter, nearby nerves may get injured or irritated producing symptoms such as a shooting type of pain down the arm; numbness; tingling; pins and needles effect; weakness of extremity; or paralysis.
- Leakage: Occasionally leakage at the insertion site may occur. Catheter Breakage: Rarely, catheter damage can occur and most often it is from improper care. If the catheter is placed in the elbow bend, breakage can also occur from repetitive motion, which should be avoided.
- **Radiologic imaging: PET-CT scans and non-contrast head CT.** A PET-CT and CT scan exposes you to radiation (discussed below). When you are in the scanner, you may experience discomfort or anxiety due to be in the small space inside the machine, or from the loud noises the scanner makes. If you become anxious or concerned in tight spaces, or from loud noises, tell the study team or technician before the scan. You may receive a medication to calm you if you need help with this.
- **Radiologic imaging: PET-CT injection of radiotracers.** A radiotracer will be injected for the PET part of the PET-CT scans. The radiation exposure for radiotracers, and for the CT component of the scan, are discussed below. Following are the risks associated with injection of contrast agents.
  - Allergic reaction, which can be severe and/or life-threatening. If you have ever had a history of severe allergies / allergic reactions, including anaphylaxis (eg, any bee-sting, food, shellfish, or nut reactions), or any previous reactions to medications; iodine; contrast agents; tape; or latex, tell the technician before the scan. After the injection and during the scan, if you experience any breathing difficulties; sweating; numbness; or heart palpitations, tell the technician immediately.
  - Kidney problems or kidney failure, especially if you are taking Glucophage (metformin, a common medicine for diabetes). Patients with kidney failure or other kidney problems should notify their physician before the scan.
  - After the injection, there is a risk of pain, discomfort, or a burning sensation at the injection site; a flushing sensation; a salty or metallic taste in the mouth; a brief headache; or nausea/vomiting. These effects usually last for a few moments. Pain, discomfort, or a burning sensation at the injection site can usually be relieved by applying moist, warm compresses to the injection site.
  - If you are a smoker or exposed to cigarettes or nicotine, you may experience spasms in the arteries of your heart.
- **Radiation from PET-CT and CT scans:** PET CT and CT scans expose you to radiation. This radiation exposure is not necessary for your medical care and is for research purposes only. The additional amount of radiation exposure is about 16.5 mSv, which is approximately equal to 33% of the limit that radiation workers (for example, a hospital x-ray technician) are allowed to receive in one year. This amount of radiation involves minimal risk and is necessary to obtain the research information desired.

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- You should notify your physician if you are pregnant, if you are lactating, or if you are breastfeeding.
- **Other risks:** Since BPM31510 is investigational (“experimental”), there may be other risks that are unknown (“unforeseeable”) at this time.
- You may experience some inconvenience due to the schedule and length of study visits, especially in the first cycle. You may be required to remain in the clinic until very late in the day to comply with the requested blood sampling schedule on some of the pharmacokinetic (PK) days in cycle 1.

**It is important that you report all symptoms and side effects that you experience as they occur, whether or not you think they are caused by the study drug BPM31510 or study procedures. Contact the [REDACTED] 650-725-8631 or via the [REDACTED]** If you are unable to reach anyone at the number(s) listed above, and you feel you may need medical attention, **call 911** or go to the nearest emergency room.

**POTENTIAL BENEFITS**

The study treatment may or may not help you. It is not possible to tell how your body will react to the study treatment. Even if you do not receive any personal benefit from the study treatment, your being in this study may, in the future, help doctors better understand and/or treat others who have the same condition as yours.

We cannot and do not guarantee or promise that you will receive any benefits from this study.

**ALTERNATIVES**

Your study doctor will discuss other possible treatment options for you. Other choices may include:

- Getting treatment or care for your cancer without being in a research study
- Taking part in another research study
- Getting comfort care guided by your symptoms. This type of care does not treat the cancer directly but may improve how you feel.

**PARTICIPANT'S RIGHTS**

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction. If you decide not to participate, tell the Protocol Director.

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You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

**ClinicalTrials.gov**

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by US Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

**CONFIDENTIALITY**

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed except as authorized by you or as required by law. However, there is always some risk that even de-identified information might be re-identified.

Patient information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

The purpose of this research study is to obtain data or information on the safety and effectiveness of BPM31150; the results will be provided to the sponsor, the Food and Drug Administration and other federal and regulatory agencies as required.

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## Authorization To Use Your Health Information For Research Purposes

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

### What is the purpose of this research study and how will my health information be utilized in the study?

This study may help the sponsor and FDA determine if development of BPM31150 should continue. Information from this study will be submitted to the company paying for the study (the drug manufacturer Berg Pharma) and international regulatory agencies including the FDA. The results from this research study are expected to be presented at scientific or medical meetings or published in scientific journals. **You will not be personally identified in the publications, although representatives of the sponsor and FDA and other international regulatory agencies may need to know who you are.**

### Do I have to sign this authorization form?

You do not have to sign this authorization form. But if you do not, you will not be able to participate in this research study, including receiving any research-related treatment. Signing the form is not a condition for receiving any medical care outside the study.

### If I sign, can I revoke it or withdraw from the research later?

If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your information (eg, necessary to maintain integrity of research). If you wish to

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revoke your authorization for the research use or disclosure of your health information in this study, you must write to:

**Seema Nagpal, MD**

Stanford Cancer Institute  
875 Blake Wilbur Dr, MC 5826  
Stanford, CA 94305

**What Personal Information Will Be Obtained, Used or Disclosed?**

Your health information related to this study, may be used or disclosed in connection with this research study, including, but not limited to identifiers such as your name and initials; address including ZIP code; phone numbers; dates including date of birth; age; biological gender (your sex); race; ethnicity; Medicare ID number; medical record number (MRN); and other numbers or codes such as your unique study identifier that might identify you. During the study, researchers will also obtain information about your health status, life-style choices, medical history, and medical diagnoses, including family medical history and allergies; your current and past medications or therapies; your physical examination results including height and weight, blood pressure readings, heart rate, breathing rate and temperature; your laboratory test results including blood, urine, and pregnancy tests; results of procedures, such as tumor measurements or assessments, medical scans including MRI, ECG, CT, and PET scans, bone marrow aspiration/biopsy; results of genetic and biomarker testing; and medical reports, such as the discharge summary and radiology, post-operative, and pathology reports. **The researchers will also get information from your medical record (includes hospital record from the Stanford Cancer Institute and your referring physician's records).**

**Who May Use or Disclose the Information?**

The following parties are authorized to use and/or disclose your health information in connection with this research study:

- ☐ The Protocol Director **Seema Nagpal, MD**
- ☐ Research Staff
- ☐ The Stanford University Administrative Panel on Human Subjects in Medical Research; the Stanford Data and Safety Monitoring

Participant ID:



**STANFORD UNIVERSITY Research Consent Form**

Protocol Director:

*IRB Use Only*

Approval Date: November 6, 2018

Expiration Date:

Protocol Title : **A Phase 1 study of BPM31510 plus vitamin K in subjects with high-grade glioma that has recurred on a bevacizumab-containing regimen**

Committee (DSMC); and/or any other unit of Stanford University as necessary

**Who May Receive or Use the Information?**

The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- ☐ Drug manufacturer Berg Pharma, or their representatives
- ☐ The Food and Drug Administration (FDA) and/or other state or international regulatory authorities
- ☐ The Office for Human Research Protections (OHRP) in the US Department of Health and Human Services (DHHS)
- ☐ The US Centers for Medicare & Medicaid Services (CMS), the agency responsible for administration of the Medicare program

Your information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

**When will my authorization expire?**

Your authorization for the use and/or disclosure of your health information will end on 31 December 2066 or when the research project ends, whichever is earlier.

**Will access to my medical record be limited during the study?**

To maintain the integrity of this research study, you may not have access to any health information developed as part of this study until it is completed. At that point, you would have access to such health information if it was used to make a medical or billing decision about you (eg, if included in your official medical record).

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Signature of Adult Participant

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Date

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Print Name of Adult Participant

Participant ID:

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## FINANCIAL CONSIDERATIONS

### Costs

If you participate in this study, the study will pay for those services, supplies, procedures, and care associated with this study that are not a part of your routine medical care. However, there may be additional costs to you. These include basic expenses like transportation and the personal time it will take to come to the Study Visits.

You and/or your health insurance must pay for services, supplies, procedures, and care that are required during this study for routine medical care. **You will also be responsible for any co-payments and/or deductibles as required by your insurance.** Participation in this study is not a substitute for health insurance.

### Payments

You will not be paid to participate in this research study. You may be reimbursed for reasonable travel expenses associated with the study visits. To discuss reimbursement and amounts please contact the study staff. Payments may only be made to U.S. citizens, legal resident aliens, and those who have a work eligible visa. You may need to provide your social security number to receive payment.

### Funding Source

Berg Pharma is paying for (sponsoring) this study, and providing the study drug BPM31150 and/or other materials for this study.

The National Institutes of Health (NIH) are providing some financial support for the facility and staff where part or all of the study is taking place.

## COMPENSATION for Research-Related Injury

All forms of medical diagnosis and treatment – whether routine or experimental – involve some risk of injury. In spite of all precautions, you might develop medical complications from participating in this study. If such complications arise, the Protocol Director and the research study staff will assist you in obtaining appropriate medical treatment. In the event that you have an injury or illness that is directly caused by your participation in this study, care will be provided to you. You will **not** be responsible for any of these costs.

If you receive Medicare benefits, and if the sponsor of this study pays for any study-related treatment, complications or injuries, personal information about you, your treatment, and your participation in this study will be provided to the sponsor, who is required by law to provide it to Medicare.

You do not waive any liability rights for personal injury by signing this form.

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**CONTACT INFORMATION**

**Questions, Concerns, Complaints, or to Report an Injury or Side Effect:** If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, [REDACTED] MD at 650-725-6000. You should also contact her at any time if you feel you have been hurt by being a part of this study.

If you are unable to reach anyone at the number(s) listed above, and you feel you may need medical attention, call or go to the nearest emergency room.

**Independent Contact:** If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at [REDACTED] or toll-free at [REDACTED]. You can also write to the Stanford IRB, Stanford University, 3000 El Camino Real, Five Palo Alto Square, 4<sup>th</sup> Floor, Palo Alto, CA 94306.

**Appointment or Alternate Contact:** If you need to change your appointment, or if you cannot reach the Protocol Director, please contact [REDACTED].

**EXPERIMENTAL SUBJECT'S BILL OF RIGHTS**

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and

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- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

Signing your name means you agree to be in this study and that you will receive a copy of this signed and dated consent form.

\_\_\_\_\_  
Signature of Adult Participant\_\_\_\_\_  
Date\_\_\_\_\_  
Print Name of Adult Participant\_\_\_\_\_  
Signature of Person Obtaining Consent\_\_\_\_\_  
Date\_\_\_\_\_  
Print Name of Person Obtaining Consent

The following witness line is to be signed only if the consent is provided as a summary form and accompanied by a short form foreign language consent.

\_\_\_\_\_  
Signature of Witness\_\_\_\_\_  
Date\_\_\_\_\_  
Print Name of Witness

(e.g., staff, translator/interpreter, family member)

- Translated short form must be signed and dated by both the participant (or their LAR) AND the witness.
- The English consent form (referred to as the "Summary Form" in the regulations):
  - Must be signed by the witness AND the Person Obtaining Consent (POC).
  - The non-English speaking participant/LAR does not sign the English consent.
  - The non-English speaking participant/LAR should not sign the HIPAA participant line
  - If the participant or the LAR is non-English speaking, the Person Obtaining Consent (POC) must ensure that 1) the LAR's Description of Authority is completed and 2) that any questions or options presented by the consent form are documented and initialed by the POC on the Summary Form, per the participant's wishes, as they are understood during the consent process.

Participant ID: \_\_\_\_\_